evidence for the occurrence of this same defect in infants and adult man. The finding that a lack of glucuronyl transferase activity exists in the newborn mouse(18) suggests that a similar lack might be a factor in the frequent occurrence of nonhemolytic jaundice in human infants.

Summary. 1. Broken-cell preparations of liver and of kidney from rats with constitutional nonhemolytic hyperbilirubinemia failed to synthesize bilirubin or *o*-aminophenol glucuronides. 2. Inhibition of β-glucuronidase with potassium saccharate failed to influence conjugation of bilirubin in these animals. 3. The evidence presented suggests that in constitutional nonhemolytic hyperbilirubinemia in rats, glucuronyl transferase activity is absent or inhibited.

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Blood Pressure in Apparently Healthy Aged 65 to 106 Years. (22980)

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A study of the range of the blood pressure in a large group of apparently healthy white Americans, 65 years of age and over, has just been completed. Little reliable information on this matter has hitherto been available. Previous studies were based on an inadequate number of subjects or covered an unrepresentative sample, of whom an unknown proportion suffered from cardiovascular disease. Little information also has been available on blood pressure in persons over 90 years of age. The study was conducted by means of questionnaires sent to physicians throughout the U.S. It was designed to insure that the population sample would 1) be large enough, 2) be widely distributed throughout the country, 3) cover a proper proportion of rural and urban dwellers, 4) be representative of various ethnic and economic groups, and 5) include only apparently healthy ambulatory people, living in the community, able to take complete care of themselves and without evidence of cardiovascular disease. The blood pressure data which have been obtained, therefore, characterize this select, active, healthy group. As such it is not a random population sample as would be obtained, for example, if every tenth person in the country had been studied.

Data gathered in such a random fashion would not, it is felt, answer the basic question of what range of blood pressure is comparable with, or is found in, active good health. The blood pressure in old people with heart disease and in institutions is being studied and the results will be published later. To minimize fluctuations in the blood pressure caused by emotional factors, the physicians were advised to take the patient's pressure after a short period of relaxation, to maintain a "matter-of-fact" attitude, and to record a newly taken pressure which had been carefully read to the nearest 2 mm Hg. In addition to the blood pressure reading, information was gathered on the geographic location of the community, and its size and nature, on the ethnic origin (place of birth) of the subject, on his height without shoes, his weight in the semi-nude, his occupation, employment or retirement, the degree of his physical activity and mental alertness, and the previous maximum blood pressure, if known. The geographic distribution of the subjects was comparable with that of all white persons, 65 years of age and over(1). There was a slight over-representation of subjects from the Northeastern States, but, since the mean values and standard deviations obtained from the 6 customary geographic areas of the United States(1) were similar, it was not considered necessary to "weight" the data in this regard. Of the 15,000 who had been examined, 5,757 (2998 males and 2759 females) were considered apparently healthy, as defined above. Analysis of the mean blood pressure and the standard deviation showed a high degree of homogeneity in the data from the various sources. These consisted of 1) individual practicing physicians, 2) members of the American College of Physicians, 3) members of the American Heart Assn., 4) physicians employed in Union Health Centers, 5) members of the American College of Chest Physicians, and 6) members of the Veterans' Administration. Since both the geographic and physician sources proved to be reasonably free from bias, this is the first study of an adequate number of apparently healthy white persons 65 years and older.

Statistical analysis. Arithmetic means, standard deviations, median and modal values were calculated for each sex, in each 5 year age group, from the 65th through the 94th year, and in the entire group 95 years of age and older. The statistical reliability of differences between mean values was determined from a computation of the standard error of the respective means. Frequency distribution graphs of the systolic and diastolic pressure of each sex in each 5 year age group were constructed. The tendency of physicians to record the blood pressure at the nearest zero, which was found in other large surveys(2a, 2b) was here, too, encountered. To minimize this artifact, class intervals of 10 mm Hg were adopted, with blood pressure readings ending in zero placed at the center of each interval. Thus, the systolic class intervals ranged from 85-94, 95-104, etc., up to 245-254. All values below 85 mm Hg systolic, and below 45 mm Hg diastolic, were each included in a single class interval. On the charts each class interval was entered at its zero midpoint, *e.g.*, 90, 100, etc.

Results. A. *Mean Pressure.* The mean systolic and diastolic pressures, and the standard deviations, calculated separately for each sex, in each 5 year age group, are shown in Table I. Unlike the trend at ages under 65, the mean blood pressures, both systolic and diastolic, *do not show a continuous rise* with age after 65. In men, the *average sys-*

TABLE I. Mean Blood Pressure of Apparently Healthy Aged People, 65 to 106 Years.

Age group	No. cases	Systolic	Diastolic
		Males	
65- 69	911	143 ± 26.0*	83 ± 9.9*
70- 74	694	145 ± 26.3	82 ± 15.3
75- 79	534	146 ± 21.6	81 ± 12.9
80- 84	385	145 ± 25.6	82 ± 9.9
85- 89	325	145 ± 24.2	79 ± 14.9
90- 94	121	145 ± 23.4	78 ± 12.1
95-106	25	146 ± 27.5	78 ± 12.7
		Females	
65- 69	856	154 ± 29.0	85 ± 13.8
70- 74	682	159 ± 25.8	85 ± 15.3
75- 79	464	158 ± 26.3	84 ± 13.1
80- 84	344	157 ± 28.0	83 ± 13.1
85- 89	263	154 ± 27.9	82 ± 17.3
90- 94	122	150 ± 23.6	79 ± 12.1
95-106	28	149 ± 23.5	81 ± 12.5

* ± stand. dev.

TABLE II. Values for Mean Pressures of All Apparently Healthy Aged People 65 to 106 Years.

Males	Systolic	Coeff. of variation, %	Diastolic	Coeff. of variation, %
2998	145 ± 22.3*	15.4	82 ± 10 *	12.2
Females				
2759	156 ± 28.0	18.0	84 ± 14.7	17.5

* ± stand. dev.

tolic shows a small increase of 2-3 mm between ages 65-69 and the 70's, actually to 146 mm Hg, but thereafter is virtually stationary. In women the increase in systolic between 65-69 and 70-74, is somewhat larger—5 mm to 159 mm Hg, but thereafter the averages decrease steadily, and after age 90 are below the average for 65-69. The *average diastolic pressure* in both sexes shows little variation from ages 65 to 80, and tends to decline thereafter. The average attains a maximum in men at ages 65-69, *viz.* 83 mm Hg, and in women at ages 65-74, *viz.* 85 mm Hg. Though some variation in the *standard deviation* of systolic and diastolic pressure occurs among the various 5 year age groups, no systematic trend or age specific relationship exists. The mean systolic and diastolic pressures of each sex, as well as the standard deviation and coefficients of variation, have been determined for the entire sample population. These values are shown in Table II. The mean blood pressure of all the men was 145/82, of all the women, 156/84. In women, the systolic pressure is definitely higher and the diastolic pressure slightly higher than in men; the standard deviation and coefficient of variation are greater. The pulse pressure in women was 72 mm Hg and in men it was 63 mm Hg.

B. *Frequency Distribution Curves.* Frequency distribution curves of the systolic and diastolic pressure have been constructed for each sex, in 5 year age groups between 65 and 94, and one for those 95 and over (Fig. 1). All the curves have a basic bell-shaped pattern, which is associated with many biologic phenomena, although in common with some of them, most of the blood pressure curves are somewhat skewed to the right. This skewness is approximately the same for all

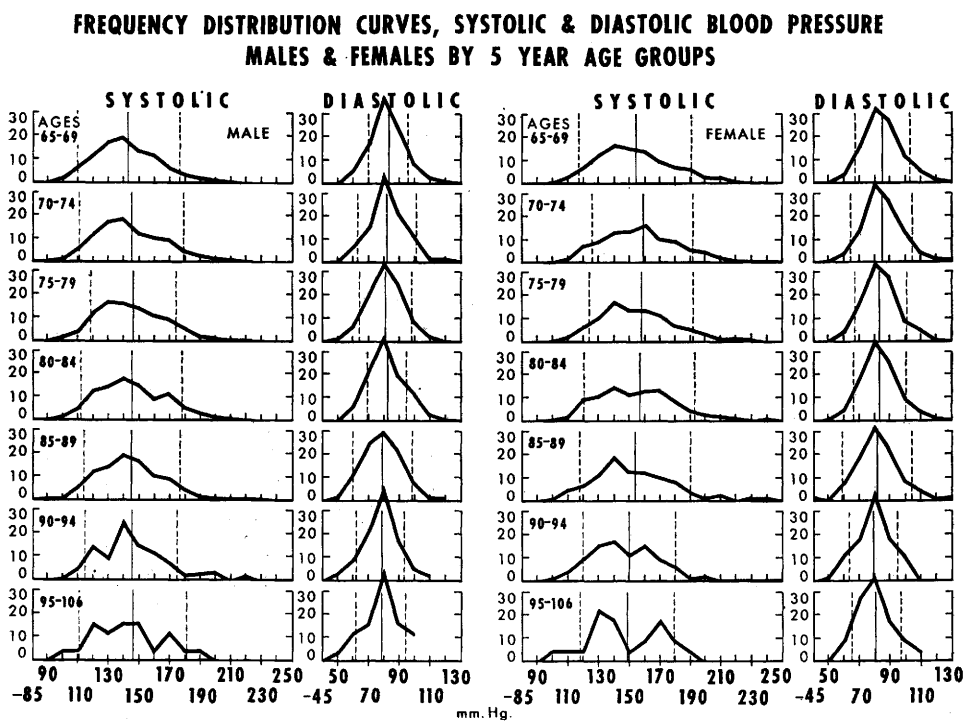

FIG. 1.

ages from 70 to 106 years of age, and thus differs from that found below the age of 65, and particularly between the ages of 45 and 64. During this age period the deviation of the blood pressure to the right progressively increases with age(3). The solid vertical line near the center of each curve represents the mean pressure; the 2 dotted vertical lines on either side of the mean, comprise in the area ± 1.282 sigma around the mean. This area includes approximately the middle 80% of all the values. In both sexes, all the *systolic pressure* curves have a positive skewness. In the males, they remain practically unchanged in basic contour at all ages, but in females, there are some minor changes. In females, also, there is a somewhat greater degree of skewness than in males at all ages over 65, and the middle 80% range is wider. The curves of the *diastolic pressure* of both sexes show no change in their basic characteristics with advancing age. In women, there is a somewhat greater dispersal of values from the mean.

C. *Range of Blood Pressure.* Two sets of limits have been calculated for systolic and diastolic pressure: the first includes all readings within ± 1.282 sigma of the mean, and the second includes all the readings within ± 2 sigma of the mean. The latter area encompasses approximately the middle 95% of all the values. Readings beyond the 2 sigma limit are outside the usual limits of variability and in our clinical experience are abnormal. Calculations of these 2 limits were made separately for each sex in each age group. There were no significant changes with age in the diastolic pressure range in either sex, or in the systolic pressure range in males. The female systolic limits showed variations of minor degree. Accordingly, in proposing practical standards of blood pressure for general use, a single set of standards for each sex is applicable to all ages, 65 and over, and these have been computed from the data and are shown in Table III. The blood pressure values have been adjusted very slightly to the figures customarily used by physicians in recording blood pressures. On this basis the middle 80% range for males is $\frac{115\text{-}175}{70\text{-}95}$; for females it is $\frac{120\text{-}192}{65\text{-}102}$. The middle 95% range for males is $\frac{100\text{-}190}{62\text{-}102}$; for females it is $\frac{100\text{-}212}{55\text{-}112}$.

TABLE III. Range of Blood Pressure in Apparently Healthy, Aged 65 to 106 Years.

	Systolic (mm Hg)		Diastolic (mm Hg)	
	♂	♀	♂	♀
Middle 80% (± 1.282 sigma)	115-175	120-192	70- 95	65-102
Middle 95% (± 2 sigma)	100-190	100-212	62-102	55-112

Values have been very slightly adjusted to conform with readings customarily used by physicians.

Discussion. The peak average systolic blood pressure is reached before age 75 and the peak average diastolic before age 70. The reason for the absence of further increase in old age can only be speculated upon. It is probable that persons with high blood pressure, as they grow old, develop clinical cardiac disease at an increasingly rapid rate and a decreasing proportion of them, therefore, are found among the apparently healthy without heart disease, which alone are included in the present study. The selective factors in morbidity and mortality tend to maintain a constant or declining pressure in healthy old age.

The higher systolic pressure found in women in this study has been reported previously(4). This sex difference is first observed at about the age of 45, and is more or less coincident with the average age of onset of menopause. However, the fact that healthy women have higher pressures on the average than men, and yet have a longer life expectancy, indicates that a single set of blood pressure standards cannot be used for both sexes.

Summary. 1) A study has been made of the blood pressure in 2,998 males and 2,759 females, 65 to 106 years of age, who were apparently healthy and without known heart disease. 2. The mean blood pressure was 145 82 for men and 156 84 for women. 3. The mean systolic and diastolic blood pressures do not show a continuous rise with age after 65. In men the *peak systolic* is 145-146 mm Hg, in women, 159 mm Hg. After the

age of 74, the systolic pressure declines slowly in women, but remains essentially constant in men. 4. The mean *diastolic pressure* shows little variation from ages 65 to 80, and tends to decline thereafter. 5. *Frequency distribution curves* of systolic and diastolic pressures, at all ages, have the basic pattern of a bell-shaped curve. In both sexes, the curves have a positive skewness larger and more consistent in the systolic than in the diastolic pressures. 6. A single set of blood pressure standards has been computed for each sex, applicable to the entire apparently healthy population from age 65 to over 100. These computations place the middle 80% range ($\pm$ 1.282 sigma) in males at $\frac{115\text{-}175}{70\text{-}95}$, and females $\frac{120\text{-}192}{65\text{-}102}$; and the middle 95% range ($\pm$ 2 sigma) in males is $\frac{100\text{-}190}{62\text{-}102}$, in females $\frac{100\text{-}212}{55\text{-}112}$.

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Turnover and Nature of Fecal Bile Acids in Germfree and Infected Rats Fed Cholic Acid-24-^{14}C. Bile Acids and Steroids 41.*† (22981)

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The turnover of bile acids has been studied in normal rats(2) and in rats treated with chemotherapeutics(3). It was found that the rate of excretion was much slower in rats treated with chemotherapeutics than in normal animals. The purpose of the present investigation was to study excretion of cholic acid in rats reared in germ-free conditions from birth and in rats with a known intestinal flora. Furthermore, the nature of the fecal acids excreted after feeding 24-^{14}C-cholic acid was to be studied as a complement to earlier experiments carried out on normal rats(4), on rats treated with chemotherapeutics(5) and *in vitro* with microorganism isolated from rat feces(6).

Methods. The germfree rats used had been delivered into the germfree unit through cesarian section and hand-fed for the first 20 days according to the technic of Gustafsson (7) with slight modifications. Litter mates were reared outside the units on the same sterilized diet. The animals used were 3-6 months old. 3 germfree and 3 control animals were studied. The diet contained casein 22%, wheat starch 63%, arachis oil 10%, salt mixture 4% and sufficient amounts of vitamins. The diet was mixed with 50% water and autoclaved at 121°C for 20 minutes. 1-2 mg of sodium salt of cholic acid-24-^{14}C(8) (3.9 μc/mg) was autoclaved in water solution, transferred to the apparatus and given by mouth to the animals. The rats were kept in metabolic cages and their feces collected every 24 hours. The

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